REMARKS

FORMAL MATTERS:

Claims 48-99 are pending.

None of the claims has been amended. However, for the Examiner's convenience, a complete listing of the claims with their current status is presented hereinabove.

INTERVIEW SUMMARY

Applicants wish to thank the Examiner and her supervisor for extending the courtesy of a telephonic interview to Applicants' representative, Richard A. Schwartz, on May 17, 2007.

Applicants' representative pointed out that the subject matter of newly cited US Patent 5,890,927 does not appear to be a relevant. The Examiner noted that the citation contained a typographical error. The correct patent number for the document is 5,980,927.

This account is believed to be a complete and accurate summary of the interview as required by 37 C.F.R. § 1.133. If the Examiner believes that this summary is inaccurate or incomplete, Applicants respectfully request that the Examiner point out any deficiencies in her next communication so that Applicants can amend or supplement the interview summary.

REJECTIONS UNDER §103

Claims 48-99 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Magruder et al. (U.S. Patent No. 5,057,318) (hereinafter "Magruder") combined with Nelson et al. (U.S. Patent No. 5,980,927) (hereinafter "Nelson"). This rejection is respectfully traversed.

The Office characterized Magruder as follows:

> US '318 teaches implantable osmotic drug delivery devices that can be highly loaded of beneficial agents and able to deliver active beneficial agents at a controlled rate continuously over time and over a broad range of dosage delivery rates according to predetermined time release pattern (abstract; col.3, lines 20-26, 30-34, 39-42; col.19, lines 27-30; col. 20, lines 20, 34). Example of the drugs suitable for delivery by the implantable osmotic device is analgesic (col.13, lines 60-61).

Final Office Action at page 3.

The Office recognized that Magruder does not disclose fentanyl, sufentanil, doses, and periods of delivery as presently claimed. The Office asserted that Magruder provides motivation "to use the implantable osmotic device to deliver analgesics that need continuous delivery and [to] manipulate the amount of analgesic and its period of delivery according to the specific patient need." *Ibid.*

In an effort to remedy the deficiency of Magruder, the Office cited Nelson. The Office asserted that

> US '927 teaches method for continuous administration of analgesics from implantable device for prolonged period of time up to several months (abstract; col.6, lines 66-67). The two preferred analgesics are fentanyl and sufentanil because of their high potency (col.4, lines 38-43). The amount and delivery rate of the active agent do not impart patentability to the claims, absent evidence to the contrary. It is within the skilled artisan to manipulate the amount of the active agent to achieve a specific delivery profile according to specific patient need.

Final Office Action at page 4.

The Office alleged that, therefore, it would have been obvious to use fentanyl or sufentanil in the implantable device of Magruder "to deliver analgesics at a controlled rate continuously over time and over a broad range of dosage delivery rates according to [a]

predetermined time release pattern...," as disclosed by Magruder, and to replace Magruder's amalgesics with fentanyl or sufentanil, based on the teachings of Nelson.

To establish a *prima facie* case of obviousness, there must be an *apparent* reason to combine the elements in the prior art in the fashion claimed by the Applicant. *KSR Int'l Co. v. Teleflex, Inc.*, 82 USPQ2d 1385, 1400 (U.S. 2007). "When prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *Id.* at 1395.

The Office has failed to establish a *prima facie* case of obviousness here for at least the following reasons:

First, the disclosures of the Magruder and Nelson documents are not combinable, and even if combined would not result in Applicants' claimed invention.

Unlike Magruder, and unlike the present claims, the Nelson apparatus is not a convective system. The Nelson device is a polymeric matrix that relies upon **diffusion** for drug delivery into the spine. Convection and diffusion are different modes of delivery. Convection involves an active process of conveying (such as via a pump), whereas diffusion does not.

Therefore, combining the Magruder and Nelson documents would change the principle of operation of Nelson in that it would involve delivery of fentanyl or sufentanil in a manner not intended by Nelson, namely via a convective system. As pointed out at MPEP § 2143.01(VI), if the proposed combination of documents changes the principle of operation of the prior art invention being modified, the teachings of the prior art are insufficient to render claims *prima facie* obvious.

Furthermore, Magruder's device is not intended to be implanted into the neuraxis (the axial unpaired part of the central nervous system, composed of the spinal cord, rhombencephalon, mesencephalon, and diencephalon), whereas Nelson's device is specifically for use in the neuraxis. Magruder discloses implantation into muscle tissue, subcutaneous space, the vaginal cavity, or the peritoneal cavity. See column 3, lines 50-56, for example.

Moreover, owing to the different sites of implantation and the different modes of delivery of Magruder and Nelson, it would not have been apparent or common sense for the routineer to

use fentanyl or sufentanil in a convective system such as that of Magruder and to have a reasonable expectation of success.

Second, as Applicants have pointed out in their prior response, Applicants' invention permits the delivery of high concentrations of fentanyl or fentanyl congener. In the fields of pharmacology and pain management at the time of applicants' priority date, no highly concentrated fentanyl/fentanyl congener formulation was available nor was there any reasonable belief or expectation that one could be attained. As disclosed in Applicants' specification, fentanyl/fentanyl congener formulations having a concentration that is substantially higher than conventional formulations have been invented by applicants, wherein the active agent can be present in up to 10,000 times or greater than the solubility of the fentanyl or fentanyl congener in aqueous solution.[1]

Applicants' ability to produce such formulations provided exceptional benefit to the art in that now, methods of pain management can be carried out by administering exceptionally small volumes of the fentanyl/fentanyl congener formulation to a site, avoiding accumulation of excessive drug at the delivery site (pooling or depot effect) since the rate of administration is at or only slightly higher than the rate of removal of the drug from the delivery site.[2]

The claimed invention is not simply about manipulating delivery volumes and concentrations of drug. Rather, the claims, by virtue of the recited delivery rates and administration periods, require use of a *concentrated* formulation of fentanyl or fentanyl congener. As the Office recognizes, these are *highly potent drugs*. Where a highly potent drug such as fentanyl or a fentanyl congener such as sufentanil is to be administered, use of a highly concentrated formulation would not have been obvious -- **especially in the context of a convective implanted device**. Instead, the natural impulse for a medical practitioner would be to use a dilute formulation containing the highly potent drug. There is simply no teaching, motivation, or suggestion in Magruder or Nelson to deliver a highly concentrated formulation of

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[1] See applicants' specification at page 18, second full paragraph through page 21, first full paragraph, and pages 35 and 36.

[2] See applicants specification at page 24, bottom paragraph.

a highly potent drug such as fentanyl or a fentanyl congener via an implantable convective delivery system.

As Applicants have pointed out previously, the methods of claims 48-99 require the delivery of an exceptionally small volume of a composition containing the fentanyl/fentanyl congener active agent, yet effective analgesia is achieved in the subject. Delivering such small volumes of drug is counter-intuitive and as such would not be considered by the routineer as part of an optimization protocol, since logically it would be expected that the pharmacological effect of the drug would drop off quickly and become negligible well before one reached the low volume rate delivery as required by Applicants' claims.

Because only Applicants' specification would have guided one to use fentanyl or sufentanil in an implantable convective delivery system, the rejection represents impermissible hindsight. Therefore, there is no apparent reason to combine the cited documents to reach Applicants' claimed invention . As such, there is no *prima facie* obviousness.

Withdrawal of this rejection is respectfully requested.

CONCLUSION

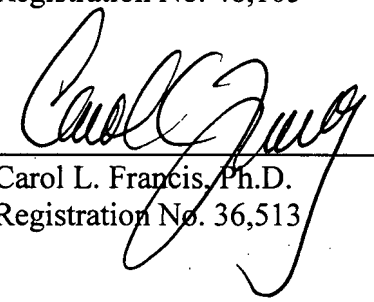
Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number DURE-007CON2.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: June 7, 2007 By: _____
Richard A. Schwartz, Ph.D.
Registration No. 48,105



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